

Appln. No. 09/441,140

Amendment dated March 17, 2005

Reply to Office action of September 17, 2004

denaturing a target polypeptide which aggregates,  
mixing the target polypeptide with said anti-  
aggregation molecule to form a mixture,  
incubating the mixture under conditions allowing for  
aggregation,  
selecting non-aggregated mixtures, and  
testing the nonaggregated target polypeptide coupled  
to the anti-aggregation molecule for bioactivity thereby  
selecting an anti-aggregation molecule with the chaperone-like  
activity of anti-aggregation which when coupled to the target  
polypeptide maintains bioactivity.

2. The method of claim 1 further characterized by  
the target polypeptide being  $\beta$ -amyloid.

3. A method of selecting an anti-aggregation  
molecule having the chaperone-like activity of anti-  
aggregation, wherein the anti-aggregation molecule is selected  
from the group consisting of a monoclonal antibody, a  
genetically engineered antibody antigen binding fragment, and  
a single chain monoclonal antibody, and wherein said anti-  
aggregation molecule binds to a bioactive native target  
polypeptide epitope with a high binding constant, reverses  
aggregation and is non-inhibitory to the biological activity  
of the target polypeptide comprising the steps of:

preparing an aggregated target polypeptide,  
mixing the target polypeptide with said anti-  
aggregation molecule to form a mixture,

Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

selecting mixtures with non-aggregated target polypeptides, and

testing the target polypeptide coupled to the anti-aggregation molecule for bioactivity thereby identifying an anti-aggregation molecule with the chaperone-like activity of anti-aggregation which when coupled to the target polypeptide maintains bioactivity.

4. The method of claim 3 further characterized by the target polypeptide being  $\beta$ -amyloid.

150. A pharmaceutical formulation, comprising a unit dose of:

(A) an antibody or antigen binding fragment thereof,  
wherein:

(i) said antibody and said fragment recognize an epitope within residues 1-28 of beta-amyloid, and

(ii) said antibody and said fragment inhibit aggregation of beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

151. The pharmaceutical formulation of claim 150,  
wherein said antibody is a monoclonal antibody.

152. The pharmaceutical formulation of claim 151,  
wherein said antibody is a human monoclonal antibody.

153. The pharmaceutical formulation of claim 151,  
wherein said antibody is a genetically-engineered monoclonal antibody.

Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

154. The pharmaceutical formulation of claim 153,  
wherein said antibody is a single-chain antibody.

155. The pharmaceutical formulation of any one of  
claims 150-154, wherein said beta-amyloid is human beta-  
amyloid.

156. A pharmaceutical formulation, comprising a  
unit dose of:

(A) an antibody or antigen binding fragment thereof,  
wherein:

(i) said antibody is obtainable using residues  
1-28 of beta-amyloid as an immunogen, and

(ii) said antibody and said fragment inhibit  
aggregation of beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

157. The pharmaceutical formulation of claim 156,  
wherein said antibody is a monoclonal antibody.

158. The pharmaceutical formulation of claim 157,  
wherein said antibody is a human monoclonal antibody.

159. The pharmaceutical formulation of claim 157,  
wherein said antibody is a genetically-engineered monoclonal  
antibody.

160. The pharmaceutical formulation of claim 159,  
wherein said antibody is a single-chain antibody.

Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

161. The pharmaceutical formulation of any one of claims 156-160, wherein said beta-amyloid is human beta-amyloid.

162. A pharmaceutical formulation, comprising a unit dose of:

(A) an antibody or antigen binding fragment thereof, wherein:

(i) said antibody and said fragment recognize an epitope within residues 1-28 of beta-amyloid, and

(ii) said antibody and said fragment maintain the solubility of soluble beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

163. The pharmaceutical formulation of claim 162, wherein said antibody is a monoclonal antibody.

164. The pharmaceutical formulation of claim 163, wherein said antibody is a human monoclonal antibody.

165. The pharmaceutical formulation of claim 163, wherein said antibody is a genetically-engineered monoclonal antibody.

166. The pharmaceutical formulation of claim 165, wherein said antibody is a single-chain antibody.

167. The pharmaceutical formulation of any one of claims 162-166, wherein said beta-amyloid is human beta-amyloid.

Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

168. A pharmaceutical formulation, comprising a unit dose of:

(A) an antibody or antigen binding fragment thereof,  
wherein:

(i) said antibody is obtainable using residues 1-28 of beta-amyloid as an immunogen, and

(ii) said antibody and said fragment maintain the solubility of soluble beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

169. The pharmaceutical formulation of claim 168, wherein said antibody is a monoclonal antibody.

170. The pharmaceutical formulation of claim 169, wherein said antibody is a human monoclonal antibody.

171. The pharmaceutical formulation of claim 169, wherein said antibody is a genetically-engineered monoclonal antibody.

172. The pharmaceutical formulation of claim 171, wherein said antibody is a single-chain antibody.

Please insert new claims 173-209 as follows:

173. The pharmaceutical formulation of any one of claims 168-172, wherein said beta-amyloid is human beta-amyloid.

174. A pharmaceutical formulation, comprising:

Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

(A) a monoclonal antibody or antigen binding fragment thereof, said monoclonal antibody being a human monoclonal antibody or a genetically engineered monoclonal antibody, wherein:

(i) said antibody and said fragment recognize an epitope within residues 1-28 of beta-amyloid, and

(ii) said antibody and said fragment inhibit aggregation of beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

175. The pharmaceutical formulation of claim 174, wherein said antibody is a human monoclonal antibody.

176. The pharmaceutical formulation of claim 174, wherein said antibody is a genetically-engineered monoclonal antibody.

177. The pharmaceutical formulation of claim 176, wherein said antibody is a single-chain antibody.

178. A pharmaceutical formulation, comprising:

(A) an antibody or antigen binding fragment thereof, wherein:

(i) said antibody and said fragment recognize an epitope within residues 1-28 of human beta-amyloid, and

(ii) said antibody and said fragment inhibit aggregation of human beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

179. The pharmaceutical formulation of claim 178,  
wherein said antibody is a monoclonal antibody.

180. The pharmaceutical formulation of claim 179,  
wherein said antibody is a human monoclonal antibody.

181. The pharmaceutical formulation of claim 179,  
wherein said antibody is a genetically-engineered monoclonal  
antibody.

182. The pharmaceutical formulation of claim 181,  
wherein said antibody is a single-chain antibody.

183. A pharmaceutical formulation, comprising:

(A) a monoclonal antibody or antigen binding  
fragment thereof, said monoclonal antibody being a human  
monoclonal antibody or a genetically engineered monoclonal  
antibody, wherein:

(i) said antibody is obtainable using residues  
1-28 of beta-amyloid as an immunogen, and

(ii) said antibody and said fragment inhibit  
aggregation of beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

184. The pharmaceutical formulation of claim 183,  
wherein said antibody is a human monoclonal antibody.

185. The pharmaceutical formulation of claim 183,  
wherein said antibody is a genetically-engineered monoclonal  
antibody.

Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

186. The pharmaceutical formulation of claim 185,  
wherein said antibody is a single-chain antibody.

187. A pharmaceutical formulation, comprising:  
(A) an antibody or antigen binding fragment thereof,  
wherein:

(i) said antibody is obtainable using residues  
1-28 of human beta-amyloid as an immunogen, and

(ii) said antibody and said fragment inhibit  
aggregation of human beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

188. The pharmaceutical formulation of claim 187,  
wherein said antibody is a monoclonal antibody.

189. The pharmaceutical formulation of claim 188,  
wherein said antibody is a human monoclonal antibody.

190. The pharmaceutical formulation of claim 188,  
wherein said antibody is a genetically-engineered monoclonal  
antibody.

191. The pharmaceutical formulation of claim 190,  
wherein said antibody is a single-chain antibody.

192. A pharmaceutical formulation, comprising:  
(A) a monoclonal antibody or antigen binding  
fragment thereof, said monoclonal antibody being a human  
monoclonal antibody or a genetically engineered monoclonal  
antibody, wherein:



Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

(i) said antibody and said fragment recognize an epitope within residues 1-28 of beta-amyloid, and

(ii) said antibody and said fragment maintain the solubility of soluble beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

193. The pharmaceutical formulation of claim 192, wherein said antibody is a human monoclonal antibody.

194. The pharmaceutical formulation of claim 192, wherein said antibody is a genetically-engineered monoclonal antibody.

195. The pharmaceutical formulation of claim 194, wherein said antibody is a single-chain antibody.

196. A pharmaceutical formulation, comprising:

(A) an antibody or antigen binding fragment thereof, wherein:

(i) said antibody and said fragment recognize an epitope within residues 1-28 of human beta-amyloid, and

(ii) said antibody and said fragment maintain the solubility of soluble human beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

197. The pharmaceutical formulation of claim 196, wherein said antibody is a monoclonal antibody.

198. The pharmaceutical formulation of claim 197, wherein said antibody is a human monoclonal antibody.

Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

199. The pharmaceutical formulation of claim 197, wherein said antibody is a genetically-engineered monoclonal antibody.

200. The pharmaceutical formulation of claim 199, wherein said antibody is a single-chain antibody.

201. A pharmaceutical formulation, comprising:  
(A) a monoclonal antibody or antigen binding fragment thereof, said monoclonal antibody being a human monoclonal antibody or a genetically engineered monoclonal antibody, wherein:

(i) said antibody is obtainable using residues 1-28 of beta-amyloid as an immunogen, and

(ii) said antibody and said fragment maintain the solubility of soluble beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

202. The pharmaceutical formulation of claim 201, wherein said antibody is a human monoclonal antibody.

203. The pharmaceutical formulation of claim 201, wherein said antibody is a genetically-engineered monoclonal antibody.

204. The pharmaceutical formulation of claim 203, wherein said antibody is a single-chain antibody.

205. A pharmaceutical formulation, comprising:

Appln. No. 09/441,140  
Amendment dated March 17, 2005  
Reply to Office action of September 17, 2004

(A) an antibody or antigen binding fragment thereof,  
wherein:

(i) said antibody is obtainable using residues  
1-28 of human beta-amyloid as an immunogen, and

(ii) said antibody and said fragment maintain  
the solubility of soluble human beta-amyloid; and

(B) a pharmaceutically acceptable carrier.

206. The pharmaceutical formulation of claim 205,  
wherein said antibody is a monoclonal antibody.

207. The pharmaceutical formulation of claim 206,  
wherein said antibody is a human monoclonal antibody.

208. The pharmaceutical formulation of claim 206,  
wherein said antibody is a genetically-engineered monoclonal  
antibody.

209. The pharmaceutical formulation of claim 208,  
wherein said antibody is a single-chain antibody.